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Pathologic and Clinical Characteristics of Elderly Patients With Breast Cancer: A Retrospective Analysis of a Multicenter Study (Anatolian Society of Medical Oncology)

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There is very little information about breast cancer characteristics, treatment choices, and survival among elderly patients. The purpose of this multicenter retrospective study was to examine the clinical, pathologic, and biologic characteristics of 620 breast cancer patients age 70 years or older. Between June 1991 and May 2012, 620 patients with breast cancer, recruited from 16 institutions, were enrolled in the retrospective study. Patients had smaller tumors at diagnosis; only 15% of patients had tumors larger than 5 cm. The number of patients who had no axillary lymph node involvement was 203 (32.7%). Ninety-three patients (15.0%) had metastatic disease at diagnosis. Patients were characterized by a higher fraction of pure lobular carcinomas (75.3%). The tumors of the elderly patients were also more frequently estrogen receptor (ER) positive (75.2%) and progesterone receptor (PR) positive (67.3%). The local and systemic therapies for breast cancer differed according to age. An association between age and overall survival has not been demonstrated in elderly patients with breast cancer. In conclusion, the biologic behavior of older patients with breast cancer differs from younger patients, and older patients receive different treatments.

Key Words: Breast cancer – Elderly patients – Clinical characteristics – Pathologic characteristics

Breast cancer is a major health problem worldwide, and its incidence is increasing.[1] Age is one of the major risk factors for breast cancer: more than 30% of all new breast cancers occur in women aged 70 years or more. Furthermore, breast cancer–related mortality increases with age.[2,3] Despite the high incidence, there is very little information about breast cancer characteristics, treatment choices, and survival among elderly patients. Elderly patients over 70 years of age have generally been excluded from randomized clinical trials of breast cancer treatments.[4]

Several studies of breast cancer biology show that older patients are estrogen receptor–positive (ER+) and/or progesterone receptor–positive (PR+), which are predictive factors of response to hormonal therapies; the treatment of these patients with endocrine therapies is the gold standard with which other systemic adjuvant treatments are compared.[5–7] Although little is known about the pathology and biology of breast cancer in older patients, many clinical trials have shown that women who develop breast cancer at an elderly age have less aggressive disease and decreased risk of recurrence.[8–11] In contrast, a few studies have demonstrated that in postmenopausal patients with hormone receptor–positive breast cancer, increasing age is associated with higher disease-specific mortality.[2,3]

The purpose of this multicenter retrospective study was to examine the clinical, pathologic, and biologic characteristics of 620 breast cancer patients age 70 years or older.

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Methods

Patient population

Between June 1991 and May 2012, 620 patients with breast cancer, recruited from 17 institutions, were enrolled into the retrospectively study. They met the following inclusion criteria: (1) they had histologically confirmed invasive breast cancer; and (2) they were 70 years or older in age. Patients who coded as having in situ tumors were excluded.

ER and progesterone receptor (PR) expression of tumors were examined by immunohistochemistry (IHC). For ER expression, tumors with >1% of the tumor cells showing nuclear staining were defined as positive. For PR expression, tumors with >10% of the tumor cells showing nuclear staining were defined as positive. HER2 positivity was assayed either by IHC, where tumors show strong and complete circumferential membranous staining in at least 30% of cells, or by fluorescent in situ hybridization (FISH).

Statistical analysis

All of the analyses were performed using the SPSS statistical software program package (version 11.5, SPSS Inc, Chicago, Illinois). The differences of the clinical characteristics in both treatment arms were analyzed by Fisher exact test. Overall survival (OS) was calculated from surgery to death. OS was calculated with the log-rank test. The Kaplan–Meier method was used to draw survival curves. The Cox proportional hazards regression model was used to determine statistically significant variables related to survival. Differences were assumed to be significant with a P value <0.05.

Results

Patient characteristics

Between June 1991 and May 2012, 620 patients with breast cancer were enrolled in this study. Overall, 620 patients (age range, 70–96 years; median age, 75.7 years) were included in this multicenter retrospective study: 291 (46.9%) were aged 70 to 74 years at diagnosis (median age, 72 years); 208 (33.6%) were aged 75 to 79 years (median age, 77 years); and 121 (19.5%) were aged 80 years or older (median age, 82 years). Elderly patients had smaller tumors at diagnosis than younger patients; only 15% of patients had tumors larger than 5 cm. The number of patients who had no axillary lymph node involvement was 203 (32.7%). Ninety-three patients (15.0%) had metastatic disease at diagnosis. Patients were characterized by a higher fraction of pure ductal carcinomas (75.3%). The tumors of the elderly patients were more frequently ER positive (75.2%) and PR positive (67.3%). The patients' baseline characteristics are listed in Table 1.

Table 1 Characteristics of patients

Characteristic	No.	%
Enrolled patients	620	
Sex		
Male	32	5.2
Female	588	94.8
Median age, years	75.7	70–96
Age		
70–74	291	46.9
75–79	208	33.6
≥80	121	19.5
PS (%)		
0–1	425	68.6
2–3	82	13.2
Unknown	113	18.2
Pathologic tumor size, mm		
<50	463	74.7
≥50	93	15.0
Unknown	64	10.3
Surgery		
Lumpectomy	65	10.5
Mastectomy	440	71.0
Unknown	115	18.5
No. of positive nodes		
0	203	32.7
1–3	174	28.1
≥4	136	21.9
Unknown	107	17.3
Estrogen receptors		
Positive	466	75.2
Negative	120	19.3
Unknown	34	5.5
Progesterone receptors		
Positive	417	67.3
Negative	167	26.9
Unknown	36	5.8
c-erbB2		
Positive	170	27.4
Negative	379	61.1
Unknown	71	11.5
Grade		
Well	76	12.3
Moderate	268	43.2
Poor	152	24.5
Unknown	124	20.0
Histology		
Ductal	467	75.3
Lobular	53	8.5
Mucinous	18	2.9
Other	71	11.5
Unknown	11	1.8
Metastasis (at diagnosis)		
Present	93	15.0

Table 2 Adjuvant therapies by age group

Characteristic	No. (%)			*P* value
	70–74 Years	75–79 Years	≥80 Years	
Adjuvant chemotherapy				
No. of patients	245	168	91	$P < 0.001$
Yes, %	69.8	63.7	34.1	
Adjuvant endocrine therapy				
No. of patients	244	168	90	$P < 0.001$
Yes, %	30.3	36.3	66.7	
Adjuvant radiation therapy				
No. of patients	268	180	106	$P > 0.05$
Yes, %	44.8	34.4	44.3	
Surgery				
No. of patients	245	156	92	$P > 0.05$
Lumpectomy, %	12.6	10.9	14.1	
Mastectomy, %	87.4	89.1	85.9	

The local and systemic therapies for breast cancer differed according to age (Table 2). There was a progressive decrease in the number of patients receiving chemotherapy according to age, with 69.8% (age 70–74 years), 63.7% (age 75–79 years), and 34.1% (age ≥80 years) ($P < 0.001$). Patients receiving endocrine therapy increased significantly with age (30.3%, 36.3%, and 66.7%, respectively; $P < 0.001$). Adjuvant radiation therapy and surgery did not have a statistically significant difference ($P > 0.05$) among patients according to age.

Survival and age

An association between age and OS has not been demonstrated in elderly patients with breast cancer. The 5-year observed and expected survivals for patients 70 to 74 years old, 75 to 79 years old, and 80 years old or older were 73%, 71%, and 76%, respectively ($P = 0.17$) (Fig. 1).

Discussion

Age is one of the major risk factors for breast cancer: more than 30% of all new breast cancers occur in women aged 70 years or more. Besides, aging causes physiologic changes in organ function and drug pharmacokinetics, which can result in reduced therapeutic benefit of chemotherapy. Thus, in older individuals, breast cancer is commonly undertreated. Furthermore, elderly patients over 70 years of age have generally been excluded from randomized clinical trials of breast cancer treatments. For this reason, breast cancer in elderly patients is a progressively widespread problem faced by the oncologist.

There is very little information about breast cancer characteristics, treatment choices, and survival among elderly patients. There are a number of published trials indicating that women who develop breast cancer at an elderly age have less aggressive disease and decreased risk of recurrence.[8,11–14] Several studies show that elderly patients had a more favorable biologic phenotype

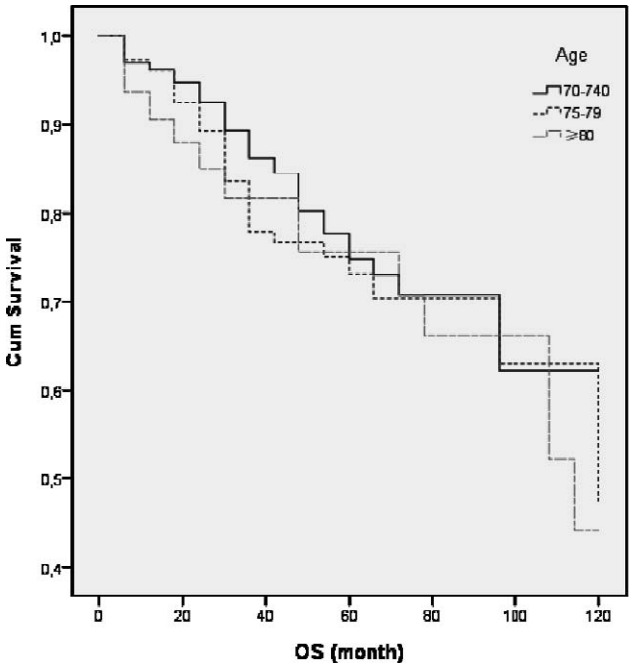

Fig. 1 Survival of patients according to age ($P = 0.17$).

such as a higher content of ER and/or PR and a lower rate of tumor-cell proliferation, and they were c-erbB2 negative as well.[2,8,13,14] These findings were similarly found in our study; the tumors of the elderly patients were also more frequently ER positive (75.2%), PR positive (67.3%), and c-erbB2 negative (61.1%).

The local and systemic therapies for breast cancer differed according to age. Previous studies indicate that elderly patients are less likely to receive systemic therapy, while elderly patients are just as likely to receive endocrine therapy as younger patients.[2,8,14–15] In the present study, the number of patients who received endocrine therapy increased significantly with age (30.3%, 36.3%, and 66.7% of patients 70–74 years old, 75–79 years old, and 80 years or older, respectively; $P < 0.001$), whereas there was a progressive decrease in the number of patients receiving chemotherapy according to age (69.8%, 63.7%, and 34.1%, respectively; $P < 0.001$). Because the frequency of presenting with ER and/or PR positive tumors increases in elderly patients, a greater proportion have been treated with adjuvant endocrine therapy.

While the incidence of breast cancer increases with age, the relationship between survival and age has not been clearly established in patients older than 70 years. Previous studies by many authors have shown that older age is associated with statistically significantly increased mortality.[2,12,17] Contrary to this, Diab *et al*[8] and Braithwaite *et al*[18] observed there was not a prognostic value of older age for survival. In our retrospective study, an association between age and OS has not been demonstrated in elderly patients with breast cancer. The 5-year observed and expected survival rates for patients age 70 to 74 years, 75 to 79 years, and ≥80 years old were 73%, 71%, and 76%, respectively ($P = 0.17$). One reason for this difference is that the present study included patients with all stages of breast cancer and did not separately evaluate patients with lymph node status and tumor size.

The present study has some limitations. First, it was retrospective in nature; second, molecular characteristics of the tumor were not evaluated; and third, the number of the patients included was rather small.

In conclusion, the biologic behavior of older patients with breast cancer is different from in younger patients, and older patients receive different treatments.

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